

Embryonic stem cells derived from in vivo or in vitro-generated murine blastocysts display similar transcriptome and differentiation potential.

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Authors: Rhodel K Simbulan, Marlea Di Santo, Xiaowei Liu, Wingka Lin, Annemarie Donjacour, Emin Maltepe, Archana Shenoy, Andrea Borini, Paolo Rinaudo

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Public Summary:

The use of assisted reproductive technologies (ART) such as in vitro fertilization (IVF) has resulted in the birth of more than 5 million children. While children conceived by these technologies are generally healthy, there is conflicting evidence suggesting an increase in adult-onset complications like glucose intolerance and high blood pressure in IVF children. Animal models indicate similar potential risks. It remains unclear what molecular mechanisms may be operating during in vitro culture to predispose the embryo to these diseases. One of the limitations faced by investigators is the paucity of the material in the preimplantation embryo to test for molecular analysis. To address this problem, we generated mouse embryonic stem cells (mESC) from blastocysts conceived after natural mating (mESCFB) or after IVF, using optimal (KSOM + 5% O₂; mESCKAA) and suboptimal (Whitten's Medium, + 20% O₂, mESCWM) conditions. All three groups of embryos showed similar behavior during both derivation and differentiation into their respective mESC lines. Unsupervised hierarchical clustering of microarray data showed that blastocyst culture does not affect the transcriptome of derived mESCs. Transcriptomic changes previously observed in the inner cell mass (ICM) of embryos derived in the same conditions were not present in mESCs, regardless of method of conception or culture medium, suggesting that mESC do not fully maintain a memory of the events occurring prior to their derivation. We conclude that the fertilization method or culture media used to generate blastocysts does not affect differentiation potential, morphology and transcriptome of mESCs.

Scientific Abstract:

The use of assisted reproductive technologies (ART) such as in vitro fertilization (IVF) has resulted in the birth of more than 5 million children. While children conceived by these technologies are generally healthy, there is conflicting evidence suggesting an increase in adult-onset complications like glucose intolerance and high blood pressure in IVF children. Animal models indicate similar potential risks. It remains unclear what molecular mechanisms may be operating during in vitro culture to predispose the embryo to these diseases. One of the limitations faced by investigators is the paucity of the material in the preimplantation embryo to test for molecular analysis. To address this problem, we generated mouse embryonic stem cells (mESC) from blastocysts conceived after natural mating (mESCFB) or after IVF, using optimal (KSOM + 5% O₂; mESCKAA) and suboptimal (Whitten's Medium, + 20% O₂, mESCWM) conditions. All three groups of embryos showed similar behavior during both derivation and differentiation into their respective mESC lines. Unsupervised hierarchical clustering of microarray data showed that blastocyst culture does not affect the transcriptome of derived mESCs. Transcriptomic changes previously observed in the inner cell mass (ICM) of embryos derived in the same conditions were not present in mESCs, regardless of method of conception or culture medium, suggesting that mESC do not fully maintain a memory of the events occurring prior to their derivation. We conclude that the fertilization method or culture media used to generate blastocysts does not affect differentiation potential, morphology and transcriptome of mESCs.

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